



03/31/97

DOCKET NO.: ISIS-0710

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of:

Cook et al.

Serial No.: 07/967,267

Group Art Unit: 1803

Filed: October 27, 1992

Examiner: G. Kunz

For: OLIGONUCLEOTIDES CONTAINING 2'-O-MODIFIED PURINES

I, Joseph Lucci, Registration No. 33,307 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

On March 26, 1997

Joseph Lucci Reg. No. 33,307

APR 18 1997

GROUP 180

Assistant Commissioner
for Patents
Washington DC 20231

AMENDMENT TRANSMITTAL LETTER
AND REQUEST FOR EXTENSION OF TIME

Transmitted herewith is an amendment in the above-identified application.

- (XX) Small entity status of this application under 37 CFR 1.9 and 37 CFR 1.27 has been established by a verified statement previously submitted.
- () A verified statement claiming small entity status under 37 CFR 1.9 and 37 CFR 1.27 is enclosed.
- () Statement to Support Filing and Submission of DNA/Amino Acid Sequences in Accordance with 37 CFR §§ 1.821 through 1.825.

The fee for additional claims presented in this amendment has been calculated as follows:

				SMALL ENTITY			OTHER THAN SMALL ENTITY	
	Claims Remaining After Amendment	Highest Number Previously Paid for	No. Extra	Rate	Fee	OR	Rate	Fee
Total Claims	15-	20= (at least 20)	0	x\$11=	\$0	OR	x\$22=	\$
Indep. Claims	4-	8= (at least 3)	0	x\$40=	\$0	OR	x\$80=	\$
First Presentation Multiple Dependent Claims				+	\$130=	\$0	OR	\$260=
Total fee for added claims:					\$0			\$

(XX) Request is hereby made under 37 CFR 1.136(a) to extend the time for response to the Office Action of November 26, 1996 to and through March 26, 1997, comprising an extension of the shortened period of one months:

	SMALL ENTITY		OTHER THAN SMALL ENTITY	
One Month	XX	\$ 55		\$ 110
Two Months		\$195		\$ 390
Three Months		\$465		\$ 930
Four Months		\$735		\$1,470
Additional fee for extended response:			\$55.00	

Applicant(s) has/have not been notified that the requested extension will not be permitted. The present application is not involved in an interference declared pursuant to 37 CFR 1.207.

Total fee required

\$55.00

() Please charge my Deposit Account No. 23-3050 in the amount of \$____. This sheet is attached in triplicate.

() An extension for _____ has already been secured and the fee paid therefore of \$_____ is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request

\$55.00

(XX) A check in the amount of \$55.00 is attached. Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050.

(XX) The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 23-3050. This sheet is attached in triplicate.

(XX) Any additional filing fees required under 37 CFR 1.16 including fees for presentation of extra claims.

(XX) Any additional patent application processing fees under 37 CFR 1.17 and under 37 CFR 1.20(d).

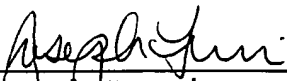
(XX) The Commissioner is hereby authorized to charge payment of the following fees during the pendency of this application or credit any overpayment to Deposit Account No. 23-3050. This sheet is attached in triplicate.

(XX) Any patent application processing fees under 37 CFR 1.17 and under 37 CFR 1.20(d).

() The issue fee set in 37 CFR 1.18 at or before mailing of the Notice of Allowance, pursuant to 37 CFR 1.311(b).

(XX) Any filing fees under 37 CFR 1.16 including fees for presentation of extra claims.

Date: March 26, 1997



Joseph Lucci
Registration No. 33,307

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On March 26, 1997

Joseph Lucci Reg. No. 33,307

#27
M. Janna
5/15/97
APR 18 1997
GROUP 180

Assistant Commissioner
for Patents
Washington, D.C. 20231

REQUEST FOR RECONSIDERATION

This responds to the Office Action mailed November 26, 1996, in connection with the above-identified patent application.

Claims 26 and 27 stand rejected under 35 U.S.C. § 103 as being unpatentable over the Buhr patent. The basis for this rejection appears to be that two references cited in the Buhr patent (i.e., the Sproat and Inoue references) allegedly disclose methods for synthesizing the claimed 2'-O-alkyl compounds. Applicants respectfully request reconsideration of the rejection, as neither the Sproat reference nor the Inoue reference teaches or suggests a synthetic route for any claimed compound.

With respect to the Sproat reference, the Office Action is incorrect in its assertion that the last line in the first

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paragraph of the references is directed to 2'-O-alkylation of guanosine (Office Action at pages 2-3). The cited text from the Sproat reference clearly is not directed to *alkylation* procedures, but, rather, to *allylation* procedures. The practice of allylation procedures would not have produced any compound defined by claims 26 and 27, and, thus, would not have rendered such compounds obvious.

The techniques alleged to be disclosed by the Inoue reference similarly would not have produced any claimed compound. The Office Action asserts that the Inoue reference teaches a means for preparing 2'-O-methyl guanosine using diazomethane. Significantly, however, 2'-O-methyl compounds are outside the scope of claims 26 and 27. Moreover, neither the Inoue reference nor any of the other art of record teaches that the diazomethane-based methods disclosed by the reference should be adapted to the synthesis of any claimed compound -- much less how such adaptation could be effected. Since neither the Inoue reference nor the Sproat reference can fairly be said to place any claimed invention in the hands of the public, reconsideration of the rejection of these claims for alleged obviousness respectfully is requested. *In re Payne*, 203 U.S.P.Q. 245, 255 (C.C.P.A. 1979) (references relied upon to support rejection under § 103 must place the claimed invention in the possession of the public).

Claims 9, 10, and 15-27 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over WO 90/08156 ("the

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Teoule reference") in view of the previously-cited Kikuchi reference. As best understood, what the Office Action asserts is that it would have been obvious to persons of ordinary skill to: (1) prepare nucleosides having the 2'-hydrocarbon groups disclosed by the Teoule references; and (2) modify such nucleosides to include the 2-aminoadenosine base disclosed by the Kikuchi reference. Applicants respectfully request reconsideration of this rejection. Even if it would have been obvious to a person of ordinary skill to make such a modification (and Applicants do not concede that it would have been obvious), the modification still would not have produced any claimed invention.

The Office Action asserts that the Teoule reference is relevant to the claimed invention for its alleged disclosure at page 4, lines 16-26 of "2'-O-nucleosides" which bear a "linear or branched, substituted or unsubstituted hydrocarbon wherein the substituents are O, S, N, NHCO, NHSO₂, SO₂, CO, alkynyl, or alkenyl." (Office Action at page 3). Significantly, however, the cited text from the Teoule reference does not teach or suggest any such "2'-nucleoside," that is, a nucleoside wherein the hydrocarbon is covalently bound to an oxygen atom which, in turn, is covalently bound to the nucleoside's 2'-position. To the contrary, the cited text from the Teoule reference teaches that the recited hydrocarbon is to be covalently bound *directly* to the 2'-position of a nucleoside -- with no intervening oxygen atom.

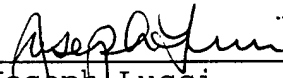
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This can be seen in the reference's teaching that R^3 (which is directly bound to the 2'-position) represents a hydrogen atom, the hydroxyl radical, a protected hydroxyl radical or the radical R^4OR^1 (Teoule reference at page 4, lines 16-17), and that R^4 , in turn, represents the hydrocarbon (*id.* at line 19). Compounds wherein hydrocarbons are directly bound to the 2'-position are clearly outside the scope of the present claims. Indeed, each of the present claims explicitly requires that an oxygen atom be directly bound to the 2'-position. Since neither the Teoule reference nor the Kikuchi reference so much as suggests such compounds, reconsideration and withdrawal of the rejection for alleged obviousness in view of such references respectfully is requested.

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Applicants submit that the claims patentably define the invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



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Date: March 26, 1997

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